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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/696,562	10/30/2003	Tae H. Ji	50229-417	5911

7590 05/31/2007

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EXAMINER	
GOUGH, TIFFANY MAUREEN	
ART UNIT	PAPER NUMBER
1657	
MAIL DATE	DELIVERY MODE
05/31/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/696,562	JI ET AL.	
	Examiner	Art Unit	
	Tiffany M. Gough	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 February 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6* is/are pending in the application.

4a) Of the above claim(s) *4-6* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed 2/20/2007 has been received and entered into the case. Claims 1-6 are pending, claims 4-6 are withdrawn and claims 1-3 have been considered on the merits. All arguments and amendments have been considered.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1,2 and 3 stand rejected under 35 U.S.C. 102 (b) as being anticipated by Grieshaber et al (Endocrinology, vol. 141, 2000).

Applicant claims a method of altering regulation of gene expression of either β-tubulin, tropomyosin-4, kinesin heavy chain or combinations thereof by contacting the genes contained within a granulosa cell, with follicle stimulating hormone (FSH) at preantral or early antral stages of development.

Grieshaber et al also teach the contacting granulosa cells with FSH to study the importance of early events of hormone signaling during FSH-induced cell differentiation, associated with the cytoskeleton (p.3462 1st full paragraph). They teach the importance FSH plays in granulosa cell differentiation and follicular development during ovulation. The early events of cell differentiation involves changes in cell morphology and cell-cell interactions, i.e cytoskeletal changes. Further, they disclose the importance of

differentiation and growth of granulose cells during the preantral period (see p.3461 1st paragraph).

Thus, the reference anticipates the claimed subject matter.

The above rejection is maintained. Applicant's arguments filed 2/20/2007 have been fully considered but they are not persuasive. Applicant argues that Grieshaber does not explicitly teach a method of altering gene expression of the claimed genes and further that it is not inherent from the disclosure that the expression of the claimed genes are regulated by FSH. Applicant merely claims altering the regulation of the claimed genes by contacting a granulosa cell, which inherently contains the claimed genes, with FSH. Thus, applicant is claiming a method of contacting a granolosa cell with FSH, which inherently contains the claimed genes. Therefore, a reference which teaches contacting a granulosa cell with FSH would inherently be altering the regulation of the claimed genes. The method does not specifically teach how the genes themselves are altered, only that they are by merely contacting the gene containing cell with FSH. Thus, applicant's arguments fail to be persuasive. The above rejection is **maintained**.

Claims 1 and 2 stand rejected under 35 U.S.C. 102 (b) as being anticipated by Ben-Ze'ev et al (Journal of Biological Chemistry, vol. 262, 1987.

Applicant claims a method of altering regulation of gene expression of either β-tubulin, tropomyosin-4, kinesin heavy chain or combinations thereof by contacting the genes contained within a granulosa cell.

Ben-Ze'ev et al teach treating granulosa cells with FSH to study organization and the expression of cytoskeletal proteins. Specifically they teach β-tubulin to be contained with the granulosa cells treated with FSH (see p.5370, 1st full paragraph). They further teach the importance and involvement of cytoskeleton in granulosa cell differentiation and development. Further, the changes in cell morphology and cytoskeleton organization associated with granulosa cell differentiation bring about changes in the expression of the respective cytoskeletal protein genes (see p.5376, 1st full paragraph).

Thus, the reference anticipates the claimed subject matter.

The above rejection is maintained. Applicant's arguments filed 2/20/2007 have been fully considered but they are not persuasive. Applicant argues that Ben-Ze'ev does not teach an alteration of expression of any of the claimed protein or β-tubulin synthesis in cells exposed to FSH. Applicant is reminded that they merely claim the alteration of either of the claimed genes when the cells which contain these genes, granulosa cells, are contacted with FSH. Thus, a reference teaching a method of contacting granulosa cells with FSH would inherently be altering the expression of either of the claimed proteins. The above rejection is **maintained**.

Claims 1 and 2 stand rejected under 35 U.S.C. 102 (b) as being anticipated by Clouscard-Martinato et al (Animal Genetics, vol. 29, 1998).

Applicant claims a method of altering regulation of gene expression of either β-tubulin, tropomyosin-4, kinesin heavy chain or combinations thereof by contacting the genes contained within a granulosa cell.

Clouscard-Martinato teach the importance of FSH in follicle development and maturation. They teach granulosa cell response to FSH by stimulating gene expression of those involved in folliculogenesis (see Introduction section). While they do not teach the alteration of the specific genes claimed by applicant, they do teach the method of altering gene expression by contacting granulosa cells with FSH.

Although, the references do not disclose the specific genes, they are contacting the granulose cell with FSH, thus, the cells must inherently contain the claimed genes.

Thus, the reference anticipates the claimed subject matter.

The above rejection is maintained. Applicant's arguments filed 2/20/2007 have been fully considered but they are not persuasive. Applicant argues that Clousard-Martinato teaches the regulation of a small percentage of genes, not all granulosa genes, while this is correct, they do teach FSH-regulated genes by contacting granulosa cells with FSH. Applicant is reminded that they merely claim the alteration of either of the claimed genes when the cells which contain these genes, granulosa cells, are contacted with FSH. Thus, a reference teaching a method of contacting granulosa cells with FSH would inherently be altering the expression of either of the claimed proteins. The above rejection is **maintained**.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

> invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Ben-Ze'ev et al (Journal of Biological Chemistry, vol. 262, 1987) or Clouscard-Martinato et al (Animal Genetics, vol. 29, 1998), or Grieshaber et al (Endocrinology, vol. 141, 2000) as supported by Kimble et al Genetics, vol.126, 1990) , along with http://www.sdbonline.orgfly/cytodkel/tubet1-1.thmhttp://pbil.univ-lyon1.fr/cgi-bin/acnuc-search-id?query=TPM4_RAT&db=Hoverprot&ide).

Applicant claims a method of altering regulation of gene expression of either β-tubulin, tropomyosin-4, kinesin heavy chain or combinations thereof by contacting the genes contained within a granulosa cell, with follicle stimulating hormone (FSH) at preantral or early antral stages of development.

Ben-Ze'ev et al teach treating granulosa cells with FSH to study organization and the expression of cytoskeletal proteins. Specifically they teach β-tubulin to be contained with the granulosa cells treated with FSH (see p.5370, 1st full paragraph). They further

teach the importance and involvement of cytoskeleton in granulosa cell differentiation and development. Further, the changes in cell morphology and cytoskeleton organization associated with granulosa cell differentiation bring about changes in the expression of the respective cytoskeletal protein genes (see p.5376, 1st full paragraph).

Clouscard-Martinato teach the importance of FSH in follicle development and maturation. They teach granulosa cell response to FSH by stimulating gene expression of those involved in folliculogenesis (see Introduction section). While they do not teach the alteration of the specific genes claimed by applicant, they do teach the method of altering gene expression by contacting granulosa cells with FSH.

Grieshaber et al also teach the contacting granulosa cells with FSH to study the importance of early events of hormone signaling during FSH-induced cell differentiation, associated with the cytoskeleton (p.3462 1st full paragraph). They teach the importance FSH plays in granulosa cell differentiation and follicular development during ovulation. The early events of cell differentiation involves changes in cell morphology and cell-cell interactions, i.e cytoskeletal changes. Further, they disclose the importance of differentiation and growth of granulose cells during the preantral period (see p.3461 1st paragraph).

Kimble et al, along with http://www.sdbonline.orgfly/cytodkel/tubet1-1.thm,teach the β-tubulin gene to be a cytoskeletal gene important in cytoskeletal reorganization and development associated within the oocyte. Tropomyosin-4 is also known to be a cytoskeletal gene (see http://pbil.univ-lyon1.fr/cgi-bin/acnuc-search-id?query=TPM4_RAT&db=Hoverprot&ide) .

None of the references specifically teach altering the regulation of gene expression of β-tubulin, tropomyosin, kinesin heavy chain or combinations thereof.

At the time of the claimed invention, it would have been obvious to one of ordinary skill in the art to contact granulosa cells with FSH and expect to see alteration of genes associated with the cytoskeleton. It is known in the art, as discussed above, that FSH plays a crucial role in cell differentiation and follicular development during ovulation, especially in early events of granulosa cells differentiation involving changes in cell morphology and cell-cell interactions, i.e the cytoskeleton. FSH is known to in the art to effect the expression of cytoskeletal proteins, i.e. cytoskeletal genes, thus, a gene such as β-tubulin, which is a cytoskeletal gene within granulosa cells would appear to inherently be altered when contacted with FSH.

Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated to observe an alteration in gene expression of genes associated with the cytoskeleton when granulosa cells, the home to such genes, are exposed to FSH because FSH is known to be important in cell differentiation and follicular development during ovulation. Cell differentiation involves changes in cell morphology and cell-cell interaction, i.e cytoskeletal changes. Thus, one would reasonably expect alteration of cytoskeletal genes expression granulose cells are contacted with FSH.

Thus, the claimed invention as a whole is prima facie obvious over the prior art.

The above rejection is maintained. Applicant's arguments filed 2/20/2007 have been fully considered but they are not persuasive. Applicant argues that the references

fail to cure the deficiencies of the art, i.e. teaching the specific genes, however, the claimed genes are known in the art to be cytoskeletal genes. FSH plays a crucial role in cell differentiation and follicular development during ovulation, especially in early events of granulosa cells differentiation involving changes in cell morphology and cell-cell interactions, i.e the cytoskeleton. FSH is known to in the art to effect the expression of cytoskeletal proteins, i.e. cytoskeletal genes, thus, a gene such as β-tubulin, which is a cytoskeletal gene within granulosa cells would appear to inherently be altered when contacted with FSH.

Applicant is reminded that they merely claim the alteration of either of the claimed genes when the cells which contain these genes, i.e. granulosa cells, are contacted with FSH. Without claiming where and how the genes are regulated, one of skill in the art would expect cells which are expressed in the granulosa gene to be altered by FSH when contacted. As written applicant claims a method of contacting a cell which expresses the claimed genes with FSH to alter the genes, thus one would say that genes are inherently being altered by simply contacting the granulosa cell with the FSH. Thus, a reference teaching a method of contacting granulosa cells with FSH would inherently be altering the expression of either of the claimed proteins. The above rejection is **maintained**.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tiffany M. Gough whose telephone number is 571-272-0697. The examiner can normally be reached on M-F 8-5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Tiffany Gough

/Ruth A. Davis/
Primary Examiner
AU 1651